Docket No. 97-52D1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Lok *et al.*: : Examiner: Kaufman. C

Serial No. 09/339,153 : Art Unit 1646

Filed June 24, 1999 :
For: MAMMALIAN ZCYTOR11

Commissioner of Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. §1.132

I Stephen R. Jaspers, Ph.D. state the following:

1. I have a Ph.D. in biochemistry.

2. I am a principal scientist in the department Genetics, ZymoGenetics, Inc., Seattle, Washington 98102, the assignee of the present application. My *curriculum vitae is* attached to the present declaration.

3. I am familiar with the subject matter of the present patent application, namely Zcytor11 polypeptide, the polynucleotide that encodes the polypeptide, the claimed invention of the present application, and antibodies that specifically bind to the Zcytor11 polypeptide.

4. I have read the Office Action dated May 30, 2001.

5. I disagree with the statement in the Office Action that the claimed invention is not supported by either a specific asserted utility or a well-established utility for the following reasons.

6. Antibodies that specifically bind to Zcytor11 are very useful to isolate cells of the pancreas that express Zcytor11. This is clearly disclosed on page 22 lines 24 – 25, and page 27 lines 21 – 22.

7. It is well within the routine skill in the art to isolate cells using antibodies once a receptor is known that is expressed by the desired cell population. The recombinant receptor can be expressed in soluble form and injected into a mammal such as a mouse or rabbit to produce polyclonal or monoclonal antibodies using techniques known by one of ordinary skill in the art. The antibodies to Zcytor11 can then be used to separate the desired or associated cells using techniques well known to one of ordinary skill in the art such as, fluorescence-activated cell sorting (FACS).

8. As evidence of this please see the accompanying exhibits. Exhibit 6, pages 156 – 159 from the text "Molecular Biology of the Cell", Alberts, B. *et al.* published by Garland Publishing, Inc. (New York, New York 1994) describe how powerful a tool an antibody that binds to a membrane-bound protein, such as Zcytor11, is to purify a population of cells that express it, and how important it is to be able to study a purified population of cells. See page 156 of Exhibit 6, which states at the beginning of the last full paragraph titled "Isolating Cells and Growing Them in Culture". The text states the following.

> Although the structure of organelles and large molecules in a cell can be seen with microscopes, a molecular understanding of a cell requires detailed biochemical analysis. Unfortunately, most biochemical procedures require large numbers of cells and begin by disrupting them. If the sample is a piece of tissue, fragments of all of its cells will be mixed together, creating confusion if the cells are of several types, which is almost always the case. In order to preserve as much information as possible about each individual type of cell, cell biologists have developed ways of dissociating cells from tissues and separating various types. The resulting, relatively homogenous population of cells then can be analyzed-either directly or after their number has been greatly increased by allowing them to proliferate in culture. (Emphasis added)

Thus, this clearly shows how necessary it is for a biochemist to work with purified, homogenous populations of cells and that an antibody to a membrane-bound protein or receptor is a powerful tool to isolate cells that express it. Thus, an antibody to Zcytor11 has a specific and substantial utility in that it can be used to produce isolated, homogenous populations of cells of the pancreas that express Zcytor11.

Exhibit 7, pages 291-305 from the text "Antibody Techniques" Malik and Lillehoj, E.P., editors , published by Academic Press (San Diego, CA, 1994), Exhibit 8, pages 28.10-28.12 from the text "Immunology"4th Ed. By Roitt, I. *et al.*, published by Mosby (London, England 1996), and Exhibit 9, pages 519-520 from the text "Cellular and Molecular Immunology, Abbas, A.K., *et al.*, published by W.B. Saunders Company (Philadelphia, PA, 2000) illustrate that antibodies that bind cell-surface antigens are very useful as tools to isolate and quantify the cells that express the cell-surface antigens. These exhibits also illustrate that it is with the routine skill in the art to isolate and quantify cells using antibodies to the cell-surface antigens. See the second

full paragraph of Exhibit 9, which states "Antibodies specific for antigens expressed on or in particular cell types are commonly used to identify these cells in tissues or cell suspensions and to separate these cells from mixed populations". Page 28.12 illustrates another method called "panning" to isolate cells using an antibody that binds to a cell-surface protein. Thus, the polynucleotides that encode Zcytor11 have a well-recognized, real-world utility to produce the Zcytor11 protein, which can be used to produce antibodies that can be used to isolate and quantify pancreatic cells that express Zcytor11.

9. I further declare that I believe all statements made herein are true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issuing thereon.

Date: 11/07/01

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EDUCATION

DEGREE	YEAR	DEPARTMENT AND INSTITUTION
B.S.	1980	Biochemistry, Washington State University, Pullman, WA
Ph.D.	1984	Biochemistry, Minor: Pharmacology University of Arizona, Tucson, AZ
Postdoctoral	1984-1991	Biochemistry and Molecular Biology, University of Massachusetts Medical Center, Worcester, MA

HONORS AND AWARDS

1997	Eureka Award, ZymoGenetics, Inc.
1987	Postdoctoral National Research Fellowship Award, National Institute of Diabetes and Digestive and Kidney Diseases
1985	Department of Biochemistry Dissertation Award University of Arizona

SUMMARY OF RESEARCH AND PROFESSIONAL EXPERIENCE

2001-present	Principal Scientist, Genetics, ZymoGenetics, Inc.
1998-2001	Principal Scientist, In Vitro Biology, , ZymoGenetics, Inc.
1996-1998	Director, Biology Network, , ZymoGenetics, Inc.
1995-1996	Assoc. Director, Diabetes Research, ZymoGenetics, Inc.
1994-1995	Senior Scientist, Diabetes Research, ZymoGenetics, Inc.
1993-1994	Scientist, Diabetes Research. ZymoGenetics, Inc.
1991-1993	Research Assistant Professor, Department of Biochemistry and Molecular Biology, University of Massachusetts Medical Center. Regulation of Glycogen Metabolism and the Function of Phosphoprotein Phosphatases in Hormone Signal Transduction.

1992-1993	Assistant Director, Peptide Synthesis/Antibody Production Core Facility, University of Massachusetts Medical Center. Coordination of peptide-protein conjugate synthesis for use in antibody production .
1985-1993	Technical Advisor/ Protein Chemist. East Acres Biologicals, Southbridge, MA. Director: Ken Pickren.
1984-1991	Postdoctoral Research Associate , Department of Biochemistry and Molecular Biology, University of Massachusetts Medical Center. Sponsor: Dr. Thomas B. Miller, Jr. Regulation of glycogen metabolism in heart and liver.
1980-1984	Graduate Research, Department of Biochemistry, University of Arizona. Advisor: Dr. Marc E. Tischler. Metabolic Responses of Skeletal Muscle to Hypokinesia/Hypodynamia. Minor: Pharmacology.
1979-1980	Undergraduate Research, Washington State University. Advisor: Dr. Michael Griswold. The effect of hormones on rat Sertoli cells in culture, testosterone metabolism in transformed cells.
1978-1979 (summer)	Laboratory Assistant-Technician; Department of Social and Health Services, State of Washington. Regional Pesticide Control Laboratory, Wenatchee, Washington. Director: Dr. A. Robbins.

PATENTS:

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Testis-specific insulin homolog proteins US 5,959,075 September 28, 1999
Human Prohormone Convertase 4 US 6,013,503 ; January 11,2000
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Methods for stimulating pancreatic islet cell regeneration US 6,114,307 September 5, 2000
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Matic, G., S. Jaspers, T.B. Miller, and A. Michelson. (1991) Platelet glycogen synthase: Further characterization and effect of insulin. Thrombosis Res. 63: 427-432.

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